

**Remarks**

No amendments have been made to the claims.

**1. Rejection under 35 U.S.C. 103(a)**

The Examiner maintains his rejection of claims 1 to 8 as allegedly obvious over EP 1024139 to Kizaki *et al.* ("Kizaki") in view of Am. Inst. Chem. Eng. J. (1984) 44(3): 612-646 to Naik *et al.* ("Naik"). The Examiner indicates that Applicants claim a process that employs a phosphonium phase transfer catalyst. According to the Examiner, Kizaki teaches a similar process that uses an ammonium phase transfer catalyst and Naik teaches that ammonium and phosphonium phase transfer catalysts are well known and commonly used. Therefore, the Examiner asserts that one of ordinary skill in the art would have known to substitute the ammonium phase transfer catalyst used in the Kizaki process with a phosphonium phase transfer catalyst to arrive at Applicants' claimed invention. In responding to Applicants' rebuttal argument in the previously filed response that Naik fails to teach that ammonium and phosphonium catalysts may be used interchangeably, the Examiner cites *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007) ("the KSR case") as effectively dispensing with this argument

"because their recognition as phase transfer catalysts creates an obvious to try situation, and applicant's invention confirms that they are in fact interchangeable."

The Examiner further cites MPEP 2144.06 in asserting that

"the issue is not whether two equivalents are recognized as interchangeable, if equivalency is recognized in the prior art, it is obvious to substitute one for the other. The recognition of the catalysts as equivalents by Naik *et al.*, creates an obvious to try situation for applicant."

Applicants submit that the Examiner's obviousness rejection appears to be based on a presumption of equivalence between the ammonium and phosphonium catalysts that is supposedly taught by Naik and an unduly narrow interpretation of the KSR case that does not accurately reflect the totality of the Court's ruling. Applicants refer to the following passage

from the KSR case upon which the Examiner appears to rely to support his “obvious to try” rejection:

When there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under §103.

Applicants submit that, as discussed below, (1) Naik does not teach that ammonium phase transfer catalysts and phosphonium phase transfer catalysts are equivalent and (2) the “obvious to try” test as defined in the KSR case has not been satisfied by the facts of the subject application. Accordingly, Applicants respectfully disagree with the Examiner’s rejection.

- (1) Naik does not teach that ammonium phase transfer catalysts and phosphonium phase transfer catalysts are equivalent

Naik is directed to a review of phase transfer catalysts and methods of modeling phase transfer catalyst reactions. Several catalysts are listed, including ammonium and phosphonium phase transfer catalysts. However, while Naik does teach that these catalysts find application in a range of industrial procedures, Naik does not teach that they may be used interchangeably in any specific process. On the contrary, Naik emphasizes a number of differences between ammonium and phosphonium phase transfer catalysts, including differences in their relative stabilities and activity characteristics (see, e.g., Table 1 on page 615 of Naik). For example, phosphonium phase transfer catalysts are less stable under basic reaction conditions while ammonium phase transfer catalysts are less stable thermally. Naik makes it clear that the selection of a phase transfer catalyst for a particular objective is typically decided by using an empirical approach in which catalysts are screened to determine their suitability for that particular objective (see, e.g., section on page 615 of Naik entitled “Choice of PT catalyst” and sentence bridging columns 1 and 2 on page 615). This teaching of an experimental approach to

choosing a catalyst with the proper characteristics is reinforced by the statement made in Naik that “the exact choice of catalyst depends on the system under consideration” (top of column 1 on page 616 of Naik) and by the recommended screening procedure involving catalysts under consideration. Accordingly, a person of ordinary skill in the art would not have an expectation of success from a reading of Naik by simply substituting an ammonium phase transfer catalyst with a phosphonium phase transfer catalyst.

The Examiner states that the issue is not whether the ammonium catalysts and phosphonium catalysts are interchangeable, but whether it would be obvious to substitute one for the other. Applicants submit that the indicated lack of interchangeability between these classes of catalysts directly influences whether it would be obvious to substitute a catalyst from one class with a catalyst from another class with any expectation of success. Naik clearly teaches that it would not be obvious to do so because of the described differences between the ammonium and phosphonium catalysts. In fact, Applicants point out that Kizaki teaches that the reaction in which the ammonium phase transfer catalyst is used is run at relatively low temperatures (see, *e.g.*, page 17, paragraph [0088] of Kizaki). As such, the thermal stability of the catalyst would not be a factor and a person of ordinary skill would instead focus on other factors, such as cost, which would favor the ammonium catalyst over the phosphonium catalyst.

(2) The “obvious to try” test as defined in the KSR case has not been satisfied in the subject application

*A. Lack of identified, predictable solutions*

The Supreme Court’s indication that obviousness exists where the solutions are predictable and where a person of ordinary skill would have good reason to pursue the known options has not been satisfied in the subject application. As discussed in section (1) above, simple substitution of a phosphonium catalyst for an ammonium catalyst in a given chemical reaction would not lead to a predictable result and as such, a person of ordinary skill would not have good reason to make this change without further evidence of potential success.

The Examiner did not comment on Applicants’ previously submitted reference by Starks (*i.e.*, Phase Transfer Catalysis, Principles and Techniques by C.M. Starks; Academic Press

(1978)) in which all successful reactions involving carboxylate ion displacement were carried out in the presence of ammonium-containing catalysts. On the few occasions where phosphonium catalysts were used, no ester product was found to be present (see (-) in “Yield %” column in Table 21). Thus, the Starks reference actually teaches away from the substitution of phosphonium phase transfer catalysts for ammonium phase transfer catalysts. Because the teaching from Starks appears in a textbook rather than in a periodical, it should be afforded greater deference from the Examiner because it more closely represents the common general knowledge of a person of ordinary skill in this art.

Further, in U.S. Patent No. 5,594,153 (a copy of which was also previously submitted for the Examiner’s review), the reaction of step (d) can be viewed as analogous to the process claimed by Applicants in the subject application, and for this procedure, ammonium salts are the catalysts of choice (see, e.g., column 6, lines 21 to 31; column 13, lines 56-60; column 15, line 16; column 16, line 62; and column 20, line 46). There is absolutely no teaching or suggestion that the reaction of step (d) should be conducted in the presence of phosphonium ions.

The previously submitted Halpern review article broadly supports the choice of ammonium-containing catalysts as a first choice for esterification reactions, which is the type of reaction recited in Applicant’s claims. All of the catalysts listed in Halpern in connection with an esterification reaction are ammonium catalysts. Halpern describes the variation between ammonium catalysts with different ligands (see, e.g., the definitions of TBAB, Aliquat 336® and TEBAC given on page 1), but there is no teaching or suggestion of any catalyst other than an ammonium-containing catalyst for use in an esterification reaction. The results provided in Halpern clearly illustrate how simply varying the ligand(s) on a catalyst can have a dramatic effect on the result achieved. The effects resulting from a more fundamental change in the catalyst – namely, changing the core nitrogen atom with a phosphorus atom – would be expected to have an even more dramatic effect, and so a person of ordinary skill in the art would not be, as a matter of procedure, likely to consider this option. Thus, Halpern can be viewed as teaching away from the casual substitution of ammonium catalysts with phosphonium catalysts. Applicants submit that the Halpern reference directly impacts the KSR “obvious to try” analysis.

As such, Applicants respectfully request that the Examiner reconsider the importance of the Halpern reference in supporting the patentability of Applicants' claims.

If one looks at other art in this area, it becomes apparent that, in relation to the reaction systems that are the focus of the subject application, the use of ammonium salts is commonly accepted. Bram *et al.*, both in Tetrahedron Letters (1982) 23: 5407-5408 and Israel Journal of Chemistry (1985) 26: 291-298 (copies of which were previously submitted for the Examiner's consideration), describe the catalysis of alkylation reactions generally, and in all cases, the catalysts used are ammonium catalysts.

Kizaki teaches the use of an ammonium phase transfer catalyst because it clearly directs a person of ordinary skill in the art toward the use of tetra n-butylammonium halides as a phase transfer catalyst for esterification reactions (see, *e.g.*, Examples 7 and 8 of Kizaki). Applicants submit that a person of ordinary skill in the art reading Kizaki would presume that the selection of an ammonium catalyst was the culmination of screening and/or optimization procedures and therefore would not have been motivated by a reasonable expectation of success to replace the ammonium catalyst with a completely different class of catalyst for which there is no prior art teaching of equivalence, as alleged by the Examiner. Applicants submit that the Examiner is engaging in prohibited hindsight analysis in asserting, against the teaching of Naik, Kizaki and the general state of the art at the time of the filing of Applicants' application, that a person of ordinary skill would substitute the relatively cheap and effective ammonium phase transfer catalyst of Kizaki with a costlier phosphonium phase transfer catalyst for which there is no reasonable expectation of success for accomplishing the same objective.

*B. No design need or market pressure to solve a problem*

According to the KSR case, the circumstances under which an "obvious to try" situation arises requires "a design need or market pressure to solve a problem...." That situation does not exist in the subject application. Kizaki provides no suggestion that are any problems associated with the use of ammonium phase transfer catalysts in the described processes that would provoke a search for alternative catalysts. In fact, on the contrary, Kizaki proclaims that the inventors' discovery of "the use of a less expensive quaternary ammonium salt in a smaller amount"

constitutes a "novel reaction technology" (page 16, paragraph 0078)). Therefore, Applicants submit that a skilled artisan would not be motivated to rely on Naik, which, as discussed above, describes the differences in outcome that can exist between phosphonium catalysts and ammonium catalysts as well as the fact that phosphonium catalysts are more expensive than ammonium catalysts (see *e.g.*, Table 1), in replacing the less expensive ammonium catalyst of Kizaki with a costlier phosphonium catalyst.

At least in view of the above discussion, Applicants submit that a person of ordinary skill in the art would not consider replacing the ammonium phase transfer catalyst of Kizaki with a phosphonium phase transfer catalyst as suggested by the Examiner. Accordingly, Applicants believe that the claims of the subject application should be acknowledged by the Examiner as nonobvious over the combination of Kizaki and Naik, resulting in the withdrawal of this rejection.


## **2. Conclusion**

The foregoing remarks are intended to convince the Examiner of the patentability of the pending claims. A favorable action is awaited. Should the Examiner find that further discussion would be of value, the Examiner is invited to telephone the undersigned at his convenience.

**EXCEPT** for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

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Respectfully submitted,  
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